

WHAT IS CLAIMED:

Subt
A1
1. A sustained-release, oral pharmaceutical formulation of tramadol, comprising a compound, formed in situ, of tramadol or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable acidic substance or a salt thereof, the compound formed in situ having a water solubility of ≤ 100 mg/ml.

2. The pharmaceutical formulation according to Claim 1, wherein the acidic substance is a pharmaceutically active substance or an auxiliary substance.

3. The pharmaceutical formulation according to Claim 1, wherein the water solubility is ≤ 50 mg/ml.

4. The pharmaceutical formulation according to Claim 3, wherein the water solubility is ≤ 30 mg/ml.

5. The pharmaceutical formulation according to Claim 4, wherein the water solubility is ≤ 10 mg/ml.

6. The pharmaceutical formulation according to Claim 1, wherein the salt of tramadol is a water-soluble salt.

7. The pharmaceutical formulation according to Claim 6, wherein the water-soluble salt is tramadol hydrochloride.

8. The pharmaceutical formulation according to Claim 1, wherein the pharmaceutically acceptable salt of the acidic substance is a water-soluble salt.

9. The pharmaceutical formulation according to Claim 8, wherein the salt of the acidic substance is selected from the group consisting of the sodium

salt of diclofenac, naproxen, acetylsalicylic acid, salicylic acid, benzoic acid, saccharin, cyclamate and acesulfame.

10. The pharmaceutical formulation according to Claim 1, wherein the tramadol or the salt of tramadol is present in excess or the acidic substance or the salt of the acidic substance.

11. The pharmaceutical formulation according to Claim 1, wherein the tramadol or the salt of tramadol is released at two or more different rates.

12. The pharmaceutical formulation according to Claim 1, wherein the tramadol or the salt of tramadol and the acidic substance or the salt of the acidic substance are present in equimolar amounts as a compound formed in situ.

13. The pharmaceutical formulation according to Claim 12, wherein the tramadol and the acidic substance are released at the same rate.

14. The pharmaceutical formulation according to Claim 1, wherein the salt of tramadol is tramadol hydrochloride and the salt of the acidic substance is diclofenac sodium.

15. The pharmaceutical formulation according to Claim 14, wherein the molar ratio of tramadol hydrochloride to diclofenac sodium ranges from 0.5:1 to 4:1.

16. The pharmaceutical formulation according to Claim 15, wherein the molar ratio of tramadol hydrochloride to diclofenac sodium is 1:1 to 2:1.

17. The pharmaceutical formulation according to Claim 14, wherein at least part of the tramadol hydrochloride and at least part of the diclofenac sodium are released at the same rate.

18. The pharmaceutical formulation according to Claim 15, wherein the tramadol hydrochloride and the diclofenac sodium are present in equimolar amounts as a compound formed in situ and both are released at the same rate.

19. The pharmaceutical formulation according to Claim 1, wherein the formulation is a multiparticulate formulation.

20. The pharmaceutical formulation according to Claim 19, wherein the multiparticulate formulation is selected from the group consisting of granules, microparticles, microtablets and pellets.

21. The pharmaceutical formulation according to Claim 19, wherein the multiparticulate formulation is filled into capsules.

22. The pharmaceutical formulation according to Claim 1, wherein the formulation is coated tablets or uncoated tablets.

23. The pharmaceutical formulation according to Claim 22, wherein the tablets are rapidly-disintegrating tablets.

24. The pharmaceutical formulation according to Claim 22, wherein the tablets comprise compressed pellets.

25. ^{further} The pharmaceutical formulation according to Claim 1, wherein the formulation comprises at least one enteric coating.

what is coated?
coating needs a substrate

26. A method for the control of pain or for the treatment of urinary incontinence, comprising administering an effective amount of the pharmaceutical formulation of Claim 1 to a patient in need thereof.

27. ✓ A method for preparing an at least partially sustained-release, oral pharmaceutical formulation, the method comprising
 mixing tramadol or a pharmaceutically acceptable salt thereof, and
 an acidic substance or a water-soluble salt thereof to form a mixture,
 moistening the mixture,
 repeating the above mixing and moistening steps and
 formulating the mixture under an energy input.

*Sunlight?
 mechanical
 heat?*

28. The method according to Claim 27, wherein the mixture is moistened with an aqueous medium.

29. The method according to Claim 28, wherein the aqueous medium is water or an aqueous binder solution.

30. The method according to Claim 27, wherein the energy input takes the form of pressure or heat, or both.

31. The method according to Claim 27, wherein the mixture is moistened and granulated more than twice and extruded at least once.

*suggests
 "further
 extruding"*

32. The method according to Claim 27, further comprising mixing an additional auxiliary substance after the mixing and moistening steps.

*into
 to
 the mixture*

with what?

33. The method according to Claim 27, wherein after the mixture is moistened, it is granulated, extruded, moistened and granulated again, extruded and then pelleted.

34. The method according to Claim 27, wherein after the mixture is moistened, it is granulated, dried, moistened and granulated again, extruded and then pelleted.

35. The method according to Claim 27, wherein the formulation is pelleted.

36. The method according to Claim 35, wherein the pellets are compressed into tablets.

37. The method according to Claim 36, wherein the pellets are provided with at least one enteric coating before being compressed.

38. The method according to Claim 27, wherein the tramadol salt is tramadol hydrochloride and the salt of the acidic substance is diclofenac sodium.

2025-01-24 14:00:00